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APPLICATION FOR U.S. LETTERS PATENT

Title:

HOMOGENEOUS, THERMOREVERSIBLE
LOW VISCOSITY POLYMANNAN GUM FILMS
AND SOFT CAPSULES MADE THEREFROM

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**HOMOGENEOUS, THERMOREVERSIBLE LOW VISCOSITY
POLYMANNAN GUM FILMS AND SOFT CAPSULES
MADE THEREFROM**

FIELD OF THE INVENTION

The present invention is directed to a homogeneous, thermoreversible gel film comprising a film forming amount of low viscosity polymannan gum, and optionally at least one of a plasticizer, a second film former, a bulking agent, and a pH controlling agent; and processes for the preparation thereof. The present invention is also directed to soft capsules and solid forms containing the gel film, as well as processes for the preparation thereof.

BACKGROUND OF THE INVENTION

Gelatin has long been used to form films useful in the preparation of soft capsules. It is a hydrolyzed protein from collagen usually obtained by boiling animal bones and cartilage under pressure with water. However, the use of gelatin suffers from several drawbacks; e.g., its animal origins often preclude its availability to those who cannot or will not take animal derived capsules and recent concerns over bovine spongiform encephalopathy, BSE, or "Mad Cow Disease."

As a result, academia and industry have been trying for many years to develop alternatives to gelatin that can desirably use many of the machines and processes, such as rotary dies, that are already in place to make soft capsules from gelatin alternatives.

For example, Japanese Patent Application Kokai Publication No. 61-10508A discloses capsules made from the composition of polysaccharides including at least carrageenan and polyhydric alcohols. Carrageenan can be used wholly or partly with

other polysaccharides such as tamarind gum, pectin, gelatin, alginates, agar, furcellaran, cellulose derivatives, locust bean gum, and guar gum. Polyhydric alcohols include sorbitol, glucose, sucrose, ethylene glycol, diethylene glycol, triethylene glycol, polyethylene glycol, propylene glycol, polypropylene glycol, butane diol and glycerin. The soft capsules are made from concave stamping dies.

Japanese Patent Application Kokai Publication No. 63-164858 discloses mixtures of polysaccharides and polyhydric alcohols with/without alkaline substances. The broad list of polysaccharides purported to be useful in the application include natural polysaccharides such as carrageenan, alginic acid, alginate derivatives, agar, locust bean gum, guar gum, tamarind seed polysaccharides, pectin, xanthan gum, glucomannan, chitin, pullulan and cyclodextrine. The polysaccharides are stated to be combined with a concentrated water solution of at least one of a polyhydric alcohol, sugar alcohol, monosaccharide, disaccharide and oligosaccharide. The mixtures are stated to be useful in forming hulls of soft capsules. The three examples are directed to making hulls of soft capsules having double layers of the mixture with gelatin and a single layer consisting of the mixture of the invention with gelatin.

U.S. Patent No. 5,089,307 discloses heat-sealable edible films comprising at least a film layer containing a water-soluble polysaccharide as the principal component, a polyhydric alcohol and water. The films are stated to be useful for sealing and packaging materials for dried foods, oily foods and the like. The polysaccharides purported to be useful include alginic acid and its salts (such as sodium salt); furcellaran; carrageenan such as kappa-, iota- and lambda-carrageenans; agar; pectin such as high-methoxy and low-methoxy pectins; gums such as tamarind seed gum, xanthan gum, guar gum, tara

seed gum, locust bean gum; pullulan; chitin derivatives such as chitosan; starch such as wheat, corn and potato starches; dextrin; edible water-soluble cellulose derivatives such as carboxymethylcellulose; and mixtures of the foregoing. The weight ratio of the polyhydric alcohol to polysaccharide is preferably used in an amount of 1:5 to 1:1, and the polysaccharide is present in an amount of not less than 50% of the total amount of active components.

U.S. Patent No. 6,331,205 discloses aqueous viscous compositions for making soft or hard capsules containing carrageenan, preferably, iota carrageenan as the single gelling agent. Iota-, lambda-, mu-, and nu-carrageenans are disclosed. Plasticizers are disclosed such as those belonging to the polyoxyls class; e.g., glycerol, sorbitol, maltodextrins, dextrose, mannitol, xylitol, polyoxyethylene glycol 400 to 6000, natural glycerides and hemisynthetics and their derivatives, etc. Soft capsules are said to be obtained by an adaptation of the "Scherer" method.

U.S. Patent No. 6,214,376 discloses gelatin-free capsules made from compositions comprising water soluble hydrophilic colloidal layers comprising gel films of kappa-carrageenan and a plasticizer. The gelatin free soft capsules are said to be made from kappa-carrageenan as the main gel-forming polymer (at least 50% by weight of gums that form thermoreversible gels or contribute to the formation of thermoreversible gels). Hydrolyzed starches such as maltodextrin may be added to increase solids concentration, aid heat sealing and prevent hazing induced by gelling salts.

U.S. Patent No. 6,340,473 discloses the use of a modified starch having a hydration temperature below about 90 °C and iota carrageenan for the manufacture of soft capsules using rotary die encapsulation apparatus. The weight ratio of the modified

starch to the iota carrageenan is stated to be crucial to forming a satisfactory film. That is, the weight ratio of the modified starch to the iota carrageenan is said to be 1.5:1. The inventors purportedly found that iota-carrageenan alone does not produce an acceptable film and that modified starch alone does not produce an acceptable film useable for encapsulation. The stated theory is that the iota carrageenan functions as an elasticizing agent rendering an otherwise inelastic, modified starch film, elastic.

It is known that certain high solids, low moisture film forming compositions containing, for example, hydrocolloids, form highly viscous solutions that make formation of hydrated films difficult to obtain. The present invention provides a process for preparing high solids, low moisture films from such highly viscous solutions.

In addition, many attempts have been made to make soft capsules from high solids, low moisture films such as hydrocolloids. However, such attempts to make soft capsules have suffered from the drawback mentioned above. That is, hydrocolloids are known to form highly viscous solutions that are difficult to sufficiently hydrate and form a film in conventional soft capsule making processes. The process of the invention therefore allows for the manufacture of soft capsules from such films.

SUMMARY OF THE INVENTION

As a first embodiment, the present invention is directed to a homogeneous, thermoreversible gel film comprising a film forming amount of low viscosity polymannan gum, e.g., low viscosity guar gum, and optionally at least one of a plasticizer, a second film former, a bulking agent, and a pH controlling agent.

As a second embodiment, the present invention is directed to a process for making gel films comprising the step of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a composition of a low viscosity polymannan gum, e.g., low viscosity guar gum, and optionally at least one of a plasticizer, second film former, bulking agent and pH controlling agent in an apparatus capable of providing sufficient shear, temperature and residence time to form a homogeneous, molten composition, wherein the temperature is at or above the solubilization temperature of the molten mass; and (ii) cooling the molten composition at or below its gelling temperature to form the gel film.

As a third embodiment, the present invention is directed to soft capsules comprising capsule walls and an encapsulated substance wherein the capsule walls comprise the gel films of the present invention, as a well as a process for the preparation thereof. The process comprises the steps of: (i) heating, hydrating, mixing, solubilizing, and, optionally, de-aerating a composition of a low viscosity polymannan gum, e.g., low viscosity guar gum and optionally at least one of a plasticizer, a second film former, a bulking agent and a pH controlling agent in an apparatus capable of providing sufficient shear, temperature and residence time to form a homogeneous, molten composition, wherein the temperature is at or above the solubilizing temperature of the molten mass; and (ii) making soft capsules directly from the molten composition or allowing the molten composition to cool to its gelling temperature or below and thereafter making soft capsules therefrom.

As a fourth embodiment, the present invention is directed to solid forms comprising a fill material encapsulated by the homogeneous, thermoreversible gel film of the present invention; e.g., hard capsules.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic of a process of the present invention to make films and soft capsules using a Stephan processor together with an extruder.

Figure 2 is a schematic of a process of the present invention to make films and soft capsules using a fluid mixing apparatus of Figure 3 and an extruder. The schematic shows the film coming out of the extruder proceeding to the encapsulation apparatus.

Figure 3 is a partially broken away, side elevational view of the fluid mixing apparatus for mixing first and second fluids with steam that can be used in the process of the present invention.

Figure 4 is another version of the schematic of Figure 2 showing the film coming out of the extruder proceeding to the encapsulation apparatus.

Figure 5 is a schematic of a process of the present invention to make films and soft capsules using the fluid mixing apparatus of Figure 3, a cooling drum and an encapsulation apparatus.

DETAILED DESCRIPTION OF THE INVENTION

The homogeneous thermoreversible gel films of the present invention utilize a film forming amount of a low viscosity polymannan gum. One example of such a polymannan gum is low viscosity guar gum. Guar gum has found utility commercially as

an emulsifier, stabilizer and thickening agent in a variety of fields. It typically has viscosity ranging from 2 to 8,000 mPas in a 1% aqueous solution at 25°C. The inventors have found that a particular type of polymannan gum, i.e., low viscosity polymannan gum (such as low viscosity guar gum) has utility in making the films and soft capsules of the present invention. A typical viscosity range for the low viscosity polymannan/guar gum of the present invention is less than 8,000 mPas, preferably, 2 to 6,000 mPas, more preferably, 2 to 4,000 mPas, more preferably, 2 to 2,000 mPas, more preferably, 2 to 1,000 mPas, more preferably, 2 to 500 mPas, more preferably, 2 to 100, mPas in a 1% aqueous solution at 25°C. It is understood that low viscosity polymannans and guar gum can also be measured at higher solids such as ULV 2 25 which has a viscosity of 25 mPas when measured at 2% solids. Such low viscosity guar gum can be obtained commercially from Indian Gum Industries, Ltd and/or their distributors as EDICOL COL ULV Guars such as ULV 2 25, ULV 25, ULV 50, ULV 100, ULV 200, ULV 500 and ULV 1000. It is understood that combinations of low viscosity polymannan/guar gums of the present invention can also be used in this invention. It is also understood that food grade enzymatically modified guar gum are in the scope of this invention.

It is noted that, e.g., guar gum is generally considered to be a “non-gelling” hydrocolloid. To the inventors’ surprise, the use of low viscosity guar gum has been shown to provide gel films having effective film strength for capsule manufacture. Here, the benefits on processing, etc. can be realized by using low viscosity guar gum.

The low viscosity polymannan/guar gum is used in the present invention in a film forming amount (e.g., an amount that adds film strength to the gel film) which is distinguished from trace amounts of low viscosity polymannan/guar gum that do not add

film properties to the film. Thus, for example, in a gel film of the present invention, a film forming amount of low viscosity polymannan/guar gum is an amount that adds film strength to the overall film. Such film forming amounts are generally at least 0.25% by weight of the dry gel film, particularly, 0.5% to 90%, more particularly, 0.5% to 50%, more particularly, 0.25 to 25% by weight of the dry gel film depending on the application.

As used herein, “homogeneous film” defines films that, to the naked eye, are visually uniform and free of defects such as lumps, cracks, particles that are undissolved that should be dissolved, non-uniform distribution of insoluble particles, etc. “Fish eyes” (mixed liquid and solid states) or “gel balls” (non-uniform gel structure) would not meet the definition of “homogeneous” as used herein.

The gel films of the present invention are homogeneous, thermoreversible gel films. They can be cast and used in a wide variety of applications as cast films or in subsequent processing.

As used herein, “thermoreversible film” defines a film that melts or flows when heated. As used herein, the melting temperature is the temperature or temperature range over which the gel film softens or flows. As used herein, the phrase “gel films” refer to thin membranes formed of structured hydrocolloid.

The gel-forming composition is characterized by a gel temperature, the temperature below which the molten mass of the gel composition must be cooled to form a self-supporting structure. Optionally, a molten mass can be cast hot and allowed to cool, as well as dry to further concentrate the solids (controlled moisture removal) until a

gel film is formed by the gel composition. The melt temperature of a thermoreversible gel film is higher than its gel temperature.

The homogeneous, thermoreversible gel film suitable for making capsules of the present invention can optionally contain at least one of a plasticizer, a second film former, a bulking agent and a pH controlling agent. The components to be added to the gel film and their amounts can vary depending on the desired use of the low viscosity guar gum gel film.

Examples of such a plasticizer include polyols such as glycerin, sorbitol, maltitol, lactitol, corn starch, fructose, polydextrose, solubilized oil, propylene glycol and polyalkylene glycols such as polyethylene glycol. The amount of the plasticizer can vary depending on the use of the gel film and its desired elasticity. For example, such plasticizers should generally be used in an amount of at least 5%, more preferably, at least 10%, more preferably, at least 20%, more preferably, at least 30% by weight of all the components including water in the dry film if a gel film having more elasticity is desired; e.g., films to be used to make soft capsules. For other applications, such as hard capsules, where less elastic films are desired, the plasticizer can be present in an amount of 0% to 20% by weight of all the components in the dry film. It is possible that the gel film of the invention contains no plasticizer at all. Examples of the second film former that can be used in the present invention include at least one of a starch, starch derivative, starch hydrozylate, cellulose gum, hydrocolloid, an alkylcellulose ether or a modified alkyl cellulose ether. Examples of the hydrocolloid include natural and synthetic hydrocolloids such as at least one of lambda carrageenans such as kappa carrageenan, kappa-2 carrageenan, iota carrageenan and less than fully modified versions thereof and

combinations thereof, polymannan gums having higher viscosities than the low viscosity polymannans of the invention, alginates, propylene glycol alginate, pullulan, gellan (including high and low-acyl gellan); dextran, and pectin. As used herein, kappa-2 carrageenan has a molar ratio of 3:6-anhydrogalactose-2-sulfate (3:6AG-2S) to 3:6-anhydrogalactose (3:6AG) content of 25 to 50%, iota carrageenan has a molar ratio of 3:6AG-2S to 3:6AG content of 80 to 100% and kappa carrageenan has a molar ratio of 3:6AG-2S to 3:6AG content less than that for kappa-2 carrageenan. For example, kappa carrageenan from *Eucheuma cottonii*, a commonly known and used seaweed source for kappa carrageenan, has a molar ratio of 3:6AG2S to 3:6AG content of less than about 10%; and iota carrageenan from *Eucheuma Spinosum*, a commonly known and used seaweed source for iota carrageenan, has a molar ratio of 3:6AG2S to 3:6AG content greater than about 85%. Kappa, kappa-2, and iota carrageenans are different from each other in both structure and functionality. If desired, where iota, kappa or kappa-2 carrageenan is used as the second film former, such carrageenan can have a viscosity of 19 cps or less, more particularly less than 10 cps, at 75 °C in a 0.10 molar sodium chloride solution containing 1.5% of the reduced molecular weight carrageenan by weight based on the total weight of the solution. This viscosity test can be performed using a Brookfield LVF (Brookfield Engineering Laboratories, Inc.) viscometer using Spindle #1 at 60 r.p.m. and determining the viscosity after six revolutions. An example of an alkylcellulose ether that can be used in the present invention is hydroxyethylcellulose. Examples of modified alkyl cellulose ethers that can be used in the present invention include hydroxypropylcellulose and hydroxypropylmethylcellulose. When the gel films of the present invention contain second film formers, the low

viscosity guar gum can be present in an amount of at least 10%, at least 40%, at least 60% or at least 80% by weight of the total amount of film formers in the dry gel film.

Note that some second film formers, such as carrageenan, can contain cations that can have positive and negative impacts on gelling properties and film strength with the carrageenan. Such beneficial cations include potassium and ammonium. These cations can be present in the carrageenan or added to it from other organic or inorganic sources. These beneficial cations can be present in an amount of less than 20% by dry weight of the carrageenan in the gel film (including water). This amount can be varied depending on the components in the system and desired melt and sealing temperatures.

Other cations, such as calcium (as mentioned above), magnesium, aluminum and chromium can adversely impact carrageenan stability and should be kept to a minimum, such as less than 10%, less than 5%, less than 1% by dry weight of the alginate in the gel film (including water).

Examples of the bulking agent include microcrystalline cellulose, microcrystalline starch, modified and unmodified starch, starch derivatives, inulin, starch hydrozylates, sugar, corn syrup and polydextrose. As used herein and in the claims, the term “modified starch” includes such starches as hydroxypropylated starches, acid-thinned starches, and the like. Examples of modified starches that can be used in the present invention include Pure Cote™ B760, B790, B793, B795, M250 and M180, Pure-Dent™ B890 and Pure-Set™ B965, all available from Grain Processing Corporation of Muscatine, Iowa, and C AraTex™ 75701, available from Cerestar, Inc. Examples of starch hydrozylates include maltodextrin also known as dextrin. Unmodified starches such as potato starch can also contribute to the film strength when combined with the hydrocolloids within the scope of

the invention. In general, modified starches are products prepared by the chemical treatment of starches, for example, acid treatment starches, enzyme treatment starches, oxidized starches, cross-bonding starches, and other starch derivatives. It is preferred that the modified starches be derivatized wherein side chains are modified with hydrophilic or hydrophobic groups to thereby form a more complicated structure with a strong interaction between side chains.

The amount of the bulking agent to be used in the present invention is generally in the amount of 0 to 20% by weight of the dry film, but more can be used, if desired, for example, at least 20%, more preferably, at least 30% of the dry film

Note that starch, starch derivatives and starch hydroxylates can be multifunctional. That is, in addition to being used as bulking agents, they can be used as second film formers. When such are used as bulking agents and second film formers, they are generally used in an amount of at least 10%, preferably, at least 20%, by weight, more preferably, at least 30% by weight of the dry gel film depending on the application; e.g., soft capsules.

Examples of the pH controlling agent to be used in the present invention include inorganic and organic bases. Preferred pH controlling agents include hydroxides, carbonates, citrates and phosphates. The pH controlling agent can be chosen as the source of added beneficial cations such as potassium. For some compositions, the pH controlling agent can be used to improve the stability of the gel film. The amount of the pH controlling agent is generally in the amount 0 to 4 %, preferably, 0 to 2 %, by weight of the dry gel film.

The dry gel films (e.g., 80% solids or higher) of the present invention have been found to have, for example, a break force of at least 1,500 grams, 2,500 grams, at least 4,000 grams, at least 5,000 grams, at least 6,000 grams, as determined using a Texture Analyzer TA-108S Mini Film Test Rig.

The films of the present invention have been found to have a solids content of at least 50%, at least 60%, at least 70%, at least 80% and at least 90% of all components in the gel film. It is understood that up to 15%, 10%, 5% water may remain strongly associated with the solids in the gel film.

Dry film thicknesses generally used for soft capsules are in the range of 0.5 to 3.0mm, more preferably, 0.8 to 1.2 mm.

It is possible that the films of the present invention can contain nonthermoreversible gums. However, so as not to adversely impact the homogeneous and thermoreversible nature of the gel films of the present invention, such nonthermoreversible films should be present in an amount of less than 50% by weight of the low viscosity guar gum, preferably, less than 40%, more preferably, less than 30%. Examples of such nonthermoreversible gums include crosslinked and partially crosslinked gums such as calcium set (e.g., crosslinked) pectins or alginates. Calcium reactive alginates and pectins, as well as their less refined forms, are considered thermoreversible gums in the absence of divalent cations. Other non-thermoreversible gums such as tragacanth gum contribute to the thermoreversability of the kappa-2 carrageenan by absorption of water within its structure thereby causing the kappa-2 carrageenan to form a denser, three-dimensional structure, as it is solubilized in less

water, providing the same effect as increasing the low viscosity polymannan/guar gum amount without the secondary film formers.

The gel films of the present invention are generally made from a process utilizing an apparatus that enables sufficiently high shear, temperature (above the gelling temperature) and residence time so as to provide a homogeneous molten mass of the composition and formation of the gel upon cooling. This is generally accomplished in the apparatus by heating, hydrating, mixing, solubilizing and optionally de-aerating the composition. Such apparatus include but are not limited to Ross mixers, Stephan processors, conventional jet cookers, extruders and the fluid mixing apparatus as set forth in Figure 3. Ross mixers, Stephan processors, extruders and conventional jet cookers are readily available commercially. Prior to cooling, the molten mass can be fed to at least one of a pump, mixer or devolatilizer. An example of a device that performs any one of such functions is an extruder. An extruded molten mass can also be directed to a film forming or shaping device (e.g. spreader box, as used in a capsule forming machine) that aids in the uniform casting of a continuous film, or, through a die that allows a direct formation of a film from the molten mass delivery equipment. Care must be taken to maintain the molten mass above the initiation of restricted flow/gel structure formation. Insulated and pre-heated (to maintain proper temperatures) transfer hoses may be used to insure molten mass flow until desired gel film formation is initiated on the casting rolls or at other film formation points, such as an extruder (restrictive flow, film forming device) or die. Additional processing methods (such as pre-heating the discharge/plunger-like head as seen in a Ross process system) can force (by pressure) the molten mass through the transfer hoses mentioned above. Additional insulation can help maintain molten mass

temperatures through the use of a Teflon disk initially placed upon the molten mass surface immediately after removing the mixing device. In addition, the feeder hoses can be introduced to the heat controlled molten mass feeder (casting) boxes located on a capsule machine either directly to the boxes or through an optional modification of the feeder boxes which introduces a top half enclosure/cover that helps maintain molten mass temperatures within the feeder box, reduces moisture loss, and maintains uniform (center) filling of the box during the extended process of forming films for capsules. It is understood that other methods of maintaining molten mass temperatures can be used to form films for capsules. This includes, but is not limited to: extrusion of the molten mass through dies/orifices into films that: can be immediately fed into the capsule forming apparatus, stored at temperatures that maintain proper film conditions (to form capsules) until needed, or dried to desired moisture, solids and texture levels, until needed. Such dried films have the property of re-absorbing water (water is introduced by any means) throughout its gel film matrix and can be rehydrated when needed, for example, to make soft capsules or other solid forms. Moisture is introduced to the film until a desired moisture content and strength/texture is reached that will allow the film's introduction into a capsule machine to make soft capsules.

As used herein, a “fluid mixing apparatus” refers to the apparatus in FIG. 3. FIG. 3 illustrates a fluid mixing apparatus **10**. The fluid mixing apparatus **10** is arranged to mix steam **2** with a first fluid or slurry **4** and a second fluid or slurry **6** to produce a molten mass or slurry mixture **8**.

The fluid mixing apparatus **10** comprises a first housing **20** having a first inlet **22** through which the steam **2** enters the housing **22**, a nozzle end **24** from which the steam **2**

exits the housing **20**, and a nozzle valve or stem **26** disposed at the nozzle end **24**. An actuator means **30** is connected to the first housing **20** for controlling the exit rate or exit pressure of the first fluid **2** at the nozzle end **24**. The actuator means **30** may be of the type manufactured by Fisher Controls U.S.A.

The fluid mixing apparatus **10** further comprises a second, mixing housing **40** coupled to the first housing **20** at the nozzle end **24** of the first housing **20**. The second housing **40** includes a second inlet **42** through which the first fluid **4** enters the second housing **40**, and a third inlet **44** through which the second fluid **6** enters the second housing **40**. The inlets **42** and **44** are disposed downstream of the first inlet **22**. As shown in FIG. 3, the second inlet **42** and third inlet **44** are disposed in a common plane and spaced apart radially from each other, most preferably directly opposite (i.e., 180° apart) about the central axis **Y** of the mixing apparatus **10**. The second housing **40** defines a generally cylindrical mixing chamber **52** that in turn defines a flow passage extending along the axial length of the mixing chamber **52** from an entry end **54** of the mixing chamber **52** to an exit end **56** of the chamber **52**. The nozzle valve **26** is movable by the actuator **30** between seated and unseated positions at the entry end **54** to control the flow rate of steam **2** into the mixing chamber **52**.

The nozzle end **24** of the first housing **20** directs the steam **2** into the entry end **54** of the mixing chamber **52**. The second inlet **42** and the third inlet **44** radially direct the first fluid **4** and second fluid **6**, respectively, into the mixing chamber **52**. The steam **2**, first fluid **4** and second fluid **6** are mixed in the mixing chamber **52** to form a molten mass or mixture **8** which exits the mixing chamber **52**. The molten mass **8** then may be

shaped into a shaped article or formed into a film, such as by casting the mixture **8** onto a cooling drum or by passing the mixture **8** through an extruder.

Referring next to FIG. 4, a system **100** for making films and capsules with the fluid mixing apparatus **10** includes a film preparation unit **60** for preparing and supplying a film **9**, and a capsule machine **80** for forming capsules **89**. The film preparation unit **60** includes: the fluid mixing apparatus **10**; a first fluid supply means **62** for supplying the first fluid **4** to the fluid mixing apparatus **10**; a second fluid supply means **64** for supplying the second fluid **6** to the fluid mixing apparatus **10**; a slurry mixture supply path **70** for supplying the molten mass or slurry mixture **8** from the fluid mixing apparatus **8** to a shaping apparatus; an optional extruder **73** in fluid communication with the mixture supply path **70** that extrudes the mixture **8** into a film **9**; a capsule machine **80** for forming capsules **89**; and a conveyor belt **90** for transporting the filled capsules **90** to a subsequent process, such as drying or packaging. The extruder **73** may be of the type manufactured by Wenger or Clextral.

The capsule machine **80** may be a conventional rotary die capsule machine of the type manufactured by R.P. Scherer Technologies of Paradise Valley, Nevada. As shown in FIG. 4, the capsule machine **80** includes a capsule product storage tank **82** that holds a capsule product **81** to be encapsulated. The capsule product **81** may include liquid, semi-liquid or powder pharmaceuticals, vitamins, nutritional supplements, paint balls, pigments, agricultural actives and pre-measured food additives. The capsule machine **80** may be coupled to one or more rollers **77**, **77'** and **78**, **78'** so that the films **9**, **9'** may be drawn into the capsule machine **80**. The film **9** is fed between heater block **86** and roller die **88**. Portions of the film **9** are drawn by vacuum into recesses formed in the surfaces

of the rotary die **88**. An amount of the capsule product **81** is delivered into the compartment formed in the film **9** by the vacuum action. Further rotary motion of the dies **88, 88'** seals the films **9, 9'** together in the nip between the rotary dies **88, 88'**. Filled capsules **89** drop into bins **87, 87'** and are presented to conveyor **90** for drying and packaging.

Referring next to FIG. 5, a capsule making system **100a** is similar to that shown in FIG. 4, wherein like reference characters refer to like elements. In FIG. 5, however, the film preparation unit **60a** includes an optional spreader box **72** and an optional cooling drum, or casting drum **74** in place of the extruder **73** of the system in FIG. 4. The system **100a** includes a fluid mixing apparatus **10** and a mixture supply path **70** to direct the slurry mixture **8** away from the fluid mixing apparatus and to the spreader box **72**. The spreader box **72** spreads the mixture **8** onto the casting drum **74**. The film **9** is formed on the casting drum **74** as the mixture **8** cools. Thereafter, the film **9** is fed to the capsule machine **80**. The film **9'** preferably is formed in the same manner as the film **9** by a second film preparation unit (not shown).

The fluid mixing apparatus **10** is adapted to produce a mixture for forming a film, more particularly an edible film for making edible capsules or strips. Incompatible film components generally are placed in different fluid inlet streams so that such incompatible components come together in the first instance at the interface of the steam injection within the mixing chamber **52** of the fluid mixing apparatus. While FIG. 3 shows inlets for steam, and first and second fluids, one or more additional inlets for one or more additional fluids may be provided. Preferably, the housings **20, 40** and other components of the fluid mixing apparatus **10** are constructed of high-grade stainless steel.

As another aspect of the invention, it is noted that the molten mass need not necessarily reach homogeneity in step (i). That is, homogeneity of the molten mass can be obtained prior to or after feeding the molten composition into at least one of the mixer, pump or devolatilizer provided the molten mass reaches homogeneity prior to gelling.

Since the gel films of the present invention have been shown to have dry film strengths of at least 2,500 grams, they are well suited to make soft capsules. Thus, the present invention is also directed to soft capsules made from the homogeneous, thermoreversible low viscosity guar gum gel films of the present invention, as well as methods of making such soft capsules.

The process for making soft capsules from the low viscosity guar gum gel films of the invention includes the use of any conventional encapsulating apparatus, e.g., a conventional rotary die apparatus or concave stamping die. For example, once the molten mass of the present invention has been made, it can be cast onto drums, cooled and then fed between rotary encapsulation dies where the films are heated again, filled, sealed and cut. For a good description of this conventional process, see WO 98/42294. Alternatively, and as a benefit of the present invention over conventional soft capsule processes, the use of the high shear apparatus disclosed above allows the molten mass to be sufficiently hydrated, applied to drums as they are cooling and then fed into conventional encapsulating apparatus for filling, sealing and cutting. This continuous type process can be used to eliminate the step of having to reheat fully gelled and cooled films for capsule preparation. The above rotary die process can be used to make soft capsules of the invention having any desired shape.

After cooling the molten composition to form the semi-gelled or fully gelled films of the invention, such films may have a moisture content of less than 50%, less than 25%, less than 15% by weight of the total components in the film prior to making soft capsules.

The fill materials for the soft capsules can be any materials widely used in the above rotary die process, including pharmaceutical ingredients, agricultural ingredients, nutraceutical ingredients, veterinary ingredients, foods, cosmetics, personal care, industrial, etc. and can be a liquid (including emulsions), suspension, dispersion, etc.

The present invention is also directed to a solid form comprising a fill material encapsulated by the homogeneous, thermoreversible gel film of the present invention. One type of such solid form is a hard capsule. Hard capsules, as used herein, refer to those solid forms that are conventionally used, e.g., in the pharmaceutical industry whereby two half shells are formed, a fill material, usually a powder, is placed in the shells and the two halves are placed together to form the hard capsule. The process for making such hard capsules would typically involve dipping metal pins or bars into the molten composition of the present invention and allowing the gel film to form around the pins. The gel films are dried and then removed from the pins. These processes are well known in the industry as methods of making hard capsules. The fill materials for the hard capsules can be any fill materials commonly used in such dosage forms. Generally, the fill materials can be liquids or solids such as powders. The fill materials can be a pharmaceutical ingredient, agricultural ingredient, nutraceutical ingredient, veterinary ingredient, food, cosmetic ingredient, etc.

The solid form may also encapsulate a powder, tablet, caplet, microcapsule or capsule in accordance with known techniques. For example, encapsulating a hard

capsule with the gel film of the invention would allow for safety seal/tamper resistant capabilities.

The gel film can also be used to modify the dissolution profile of the dosage forms. For example, gel films of the invention can contain added components that can create solid dosage forms having immediate release, controlled, enteric or delayed release capabilities. Definitions of “immediate release”, “delayed release” and “enteric” can be found in the U.S. Pharmacopeia and are incorporated herein by reference.

The present invention is now described in more detail by reference to the following examples, but it should be understood that the invention is not construed as being limited thereto. Unless otherwise indicated herein, all parts, percents, ratios and the like are by weight.

EXAMPLES

Unless otherwise indicated, the following procedures were used to prepare and evaluate the materials and films in Examples 1-3. The Stephan UMC5 processor is a laboratory scale mixing device which provided suitable high shear mixing, heating, and deaerating of the formulations which were cast as films in the laboratory. A suitable batch size used with the Stephan UMC5 processor was 1500 grams.

An aqueous starch dispersion was prepared by dissolving any salts/buffers and pH modifiers in deionized water. The starch and/or maltodextrin (M100) were added and mixed until dissolved/dispersed. Pure Cote® B760 and B790 starches are available from the Grain Processing Corporation of Muscatine, Iowa.

A hydrocolloid mixture was prepared in the Stephan UMC5 processor by premixing the plasticizers until uniform, and adding the preblended dry hydrocolloids portionwise while mixing for about 30 seconds at 200 rpm after each addition. Sorbitol Special and glycerin were used as plasticizers. Sorbitol Special is an aqueous solution of sorbitol and sorbitol anhydrides at 76% solids supplied by SPI Polyols, Inc. (New Castle, DE).

The starch dispersion was added to the non-aqueous hydrocolloid mixture and mixed at 300 rpm for 5 minutes. The mechanical agitation was increased to 2100 rpm and the mixture was heated to 85°C to 95°C with mixing. When the target temperature was achieved, the mixture was stirred for 30 minutes, then the sample was held under vacuum (50-60 bars) with continued agitation for an additional 45 minutes.

When the hold time under vacuum at temperature has been completed, the sample was poured into a preheated wide mouth quart Mason jar. Temperature and pH were recorded. Viscosity was measured on the hot sample using a Brookfield LVF viscometer.

A small portion of the sample was set aside and refrigerated usually overnight prior to measurement of gel/melt properties and solids using an Atago E series hand held refractometer (Gardco, Pompano Beach, FL). The melt temperature was determined by placing a small chunk of the refrigerated gel on a wire string stand held within a test tube so that the chunk does not contact the wall of the test tube. The test tube was covered with aluminum foil with a small hole to allow measurement of the gel temperature using a digital thermometer probe. The test tube was immersed in the heating bath so that the chunk is below the surface of a hot water bath at approximately 100°C. A silicone oil bath was used for samples that had melt temperatures above 90°C. The melt temperature

was recorded when the gelled sample became wet in appearance, softened and could be stirred (a temperature range was noted). Once the sample had melted, the test tube was transferred to a second beaker containing cold tap water (15°C). The temperature probe was used to record the temperature as the sample was cooled and to probe the sample surface to determine whether the sample had begun to gel. The gel temperature was the temperature upon cooling where the sample no longer flowed to fill in an indentation made by the probe.

The hot sample was then cast, using a draw down bar with a gap set at 3mm clearance, onto 177 mm by 177 mm by 5 mm metal plates which were pre-sprayed with PAM (lecithin) to facilitate easy removal of film material. The gel coated plates were covered to avoid loss of moisture from the cast film. Cast films were typically refrigerated (less than 8°C) for at least one-half hour prior to removal of the film for testing. Refrigeration is not required for film formation. Dried film strips were prepared by drying the coated plates in a 40 °C forced air/fan oven. Films dried 2 hours at 40°C gave an intermediate solids of about 60%, while films dried overnight at 40°C typically gave solids of 80% or higher. Test properties were measured at room temperature (approximately 20 °C) unless otherwise specified. The percent of solids of the dried film was determined between the cast film at its formulated solids level and the dried film by difference in weight. Break force (BF) was measured on the cast and dried film strips using a Texture Analyzer TA-108S Mini Film Test Rig.

Unless otherwise indicated, Maltrin M100 was obtained from Grain Processing Corporation, Pure-Cote B760 was obtained from Grain Processing Corporation, Sorbitol

Special was obtained from SPI Polyols and Glycerin was obtained from VWR (EP/USP grade).

Example 1

Table II below shows compositions and film properties for formulations prepared using low viscosity guar ULV 50 and low viscosity guar gum in combination with kappa-2 carrageenans.

Cgn A is a kappa-2 carrageenan, a natural random block co-polymer of kappa carrageenan and iota carrageenan in a ratio of 1.5 to 3.0:1, respectively, that was obtained as an alkali processed, clarified extract of *Gigartina skottsbergii*, essentially haploid (gametophyte) plants. Minor levels (under 5% total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants were also present. Cgn A has a low divalent cation content and low potassium cation content as shown in Table I.

Cgn B is a kappa-2 carrageenan that was obtained as an alkali processed, clarified extract of a mixture of *Gigartina skottsbergii* and *Sarcothalia crispata*, primarily haploid (gametophyte) plants. About 10-20% (total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants were also present.

The properties of the kappa-2 carrageenans are shown in Table 1. Viscosity of an aqueous solution at 1.5 wt % solids was measured at 75 °C using a Brookfield LVF viscometer at appropriate speeds and spindles. The properties of 2% water gels prepared using 2 wt% of samples Cgn A (#1) without added cations, (#2) with 0.2 wt% added KCl and (#3) with 0.2% added KCl and 0.2% CaCl₂, respectively, were characterized using a

TXTM Texture Analyzer. Gels were tested at 25°C and the break force (in grams) and the penetration (in millimeters) was recorded.

Table I: Properties of Kappa-2 Carrageenan

	Cgn A	Cgn B
Cation Exchange	Yes	No
Mg, %	0.05	0.05
Ca, %	0.15	0.45
K, %	0.67	13.40
Na, %	7.40	0.90
Visc, mPs	98	NT
pH	10.1	“
<u>2% water gel</u>		
BF (g)	0	“
<u>2% water gel (KCl)</u>		
BF(g)	38	“
<u>2% water gel (KCl +</u>		
<u>CaCl₂)</u>		
BF (g)	181	“

Table II. Formulations and Films Using Guar with Kappa-2 Carrageenan

	Ex 1-1	Ex 1-2	Ex 1-3	Ex 1-4	Ex 1-5
<u>Ingredients(g)</u>					
Water	836.3	836.3	836.3	836.3	836.3
Cgn B	0.0	40.5	20.3	0.0	0.0
Cgn A	0.0	0.0	20.3	40.5	40.5
GUAR ULV 50	90.0	49.5	49.5	49.5	49.5
Starch B760	220.8	220.8	220.8	220.8	220.8
Potassium Chloride	0.0	0.0	0.0	4.5	4.5
Sorbitol SP	264.4	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2	88.2
Total weight (g)	1500.0	1500.0	1500.0	1500.0	1500.0
Temp, °C*	90	90	90	87	95
Viscosity, mPa-s*	>50,000	>50,000	>50,000	>50,000	>50,000
Gel, °C	47	68-69	69	50	54-65
Melt, °C	78	85-87	86-88	67-68	76-83
PH	4.8	5.8	5.9	5.2	5.2

	Ex 1-1	Ex 1-2	Ex 1-3	Ex 1-4	Ex 1-5
Ingredients(g)					
Cast film					
Solids, est	42 %	45%	42%	40.2%	45%
BF (g)	<40	239	349	130	330
Dried film (2hr, 40°C)					
Solids, est	65%	60%	60%	63%	66%
BF (g)	722	953	2189	1194	1631
Dried film (16 hr, 40°C)					
Solids, est	86%	87%	75%	84%	84%
BF (g)	4436	7476	6901	6276	8733

*Temperature and viscosity of the molten mass prior to casting

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some showed greater strengths than others. The dried film strength at 16 hours, 40 °C for the above inventive gel films is believed to be sufficient to make soft capsules on existing machines. Moreover, the dried film strength at 2 hours, 40 °C, e.g., of Examples 1-3 to 1-5 also are sufficient to make soft capsules on existing machines. Example 1-2 demonstrates that a 55 to 45 %by weight mixture of guar with kappa-2 carrageenan has increased strength compared to guar alone (Example 1-1). Comparison of Examples 1-4 and 1-5 demonstrates the desirability of maintaining process temperatures for the molten mass above the gel temperature, as Example 1-5 provided finished (dried) gel strengths, when cast at 95 °C, at least 28% higher than a film cast at 87 °C (Example 1-4). The lower gel strength values are reflective of potential pre-gelation during film formation causing a relatively lower gel strength. All films were free of syneresis upon storage and maintained their relative flexibility.

Viscosities were generally found to be at or near the maximum for the test equipment and conditions used. Therefore, use of supplementary equipment with the

initial hydration/activation apparatus can provide additional shear and solids concentration effects while maintaining process temperatures well above their high solids set/gel temperatures ($>100^{\circ}\text{C}.$). An example of this supplementary equipment, but not limited to, would be an extruder type device sufficient to maintain adequate temperatures and shear necessary to provide the homogeneous mixing and solids concentrations necessary to allow either shaping of the molten mass for direct film or capsule casting or further allow shaping of the molten mass into a desired form such as a film either for use as a film or further processed into other forms and functions.

Example 2

The properties of films prepared by using blend compositions of low viscosity guar gum ULV50 in combination with either kappa carrageenan or kappa carrageenan and/or iota carrageenan are presented in Tables III and Table IV, respectively. The carrageenans used are described below. Carrageenan L is a kappa carrageenan having a viscosity of 10-15 cP.

Table III: Films Using Low Viscosity Guar and Kappa Carrageenan

	Ex 2-1	Ex 2-2	Ex 2-3	Ex 2-4
Ingredient (g)				
Water	836.3	836.3	836.3	836.3
Cgn L	40.5	40.5	40.5	40.5
Guar ULV 50	49.5	49.5	49.5	49.5
Starch B760	0	220.8	220.8	0
Starch B790	220.8	0	0	0
M-100	0	0	0	220.8
KCl	0	0	4.5	4.5
Sorbitol SP	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0	1500.0

	Ex 2-1	Ex 2-2	Ex 2-3	Ex 2-4
Ingredient (g)				
Temp, °C*	90	90	90	90
Viscosity, mPas*	16,000	>50,000	36,750	27,100
As Cast				
Gel, °C	36	53	57	56
Melt, °C	61	75-77	76-78	75-78
PH	5.3	5.2	5.1	5.3
Cast film				
Solids, est	41.5%	40%	45%	43%
BF (g)	170	227 g	283	217
Dried film (2 hrs@ 40°C)				
Solids, est	69%	65%	64%	66%
BF (g)	1368	1574	1144	1236
Dried film (16 hours, 40°C)				
Solids, est.	84%	85%	85%	83%
BF (g)	5541	7638	7029	5671

* Temperature and viscosity of the molten mass prior to casting

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some showed greater strengths than others.

Use of kappa carrageenan in combination with guar (Example 2-2) increased the film strength for guar alone (Example 1-1).

KCl addition (Example 2-3) increased the gel temperature and also the 40% solids gel strength. Further, KCl addition and varying ratios of film forming ingredients will control cast film strength and gel melt temperatures. When kappa carrageenans are used in combination with low viscosity guar of the invention, control of cation divalency desirably prevents/minimizes gel hardening and brittleness.

Table IV reports the compositions and properties of films formed using low viscosity guar ULV50 with kappa and iota carrageenans. Cgn C is an alkali processed

clarified kappa carrageenan extract of *Kappaphycus alvarezii* (*Eucheuma cottonii*). Cgn D is an alkali processed clarified iota carrageenan extract of *Eucheuma denticulatum* (*Eucheuma spinosum*) with low divalency. Both Cgn C and Cgn D have low divalency.

Table IV: Films Using Guar, Kappa Carrageenan, and Iota Carageenans

	Ex 2-5	Ex 2-6	Ex 2-7	Ex 2-2
Ingredient (g)				
Water	836.3	836.5	836.5	836.3
Cgn C	0	13.5	27	40.5
Cgn D	40.5	27	13.5	0
GUAR	49.5	49.5	49.5	49.5
Starch B760	220.8	220.8	220.8	220.8
Sorbitol SP	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0	1500.0
Temp, °C*	93	90	90	90
Viscosity, mPa-s*	46,100	41250	41,500	>50,000
As Cast Film				
Gel, °C	70	46	43	53
Melt, °C	85-90	65-66	56-62	75-77
pH	5.8	5.4	5.4	5.2
As Cast film				
Solids, Brix	39%	43%	41%	40%
BF (g)	102	48	95	227 g
Dried film (2 hrs @ 40C)				
Solids, est	63 %	60%	60%	65%
BF (g)	1068	282	679	1574
Dried film (16 hours, 40 C)				
Solids, est.	82%	80%	80%	85%
BF (g)	5915	6067	5549	7638

* Temperature and viscosity of the molten mass prior to casting

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some were stronger than others. The above examples show

how the addition of the other carrageenans added strength to the low viscosity guar film. Further strengthening and control of gel/melt temperatures can be achieved by adding appropriate amounts of cations.

Example 3

Table V presents compositions and properties of films formed using mixtures of guar with potassium alginates and/or carrageenans. Alginates are polyuronate copolymers comprising mannuronate (M) and guluronate(G) units. KAHG is a potassium alginate where the alginate has a high level of G units and is extracted from *Laminaria hyperborean*. KAHM is a potassium alginate where the alginate has a high level of M units and is extracted from *Lessonia trabeculata*.

Table V: Films Using Low Viscosity Guar, Potassium Alginates and Carrageenans

	Ex 3-1	Ex 3-2	Ex 3-3	Ex 3-4	Ex 3-5	Ex 3-6
Ingredient (g)						
Water	836.3	836.3	836.3	836.3	836.3	836.3
KAHG	60	60	40.5	10.5	0	0
KAHM	0	0	0	0	60.0	10.5
Cgn L	30	30	0	30	30.0	30
GUAR ULV50	0	0	49.5	49.5	0	49.5
Starch B760	220.8	220.8	220.8	220.8	220.8	220.8
Sorbitol SP	264.4	264.4	264.4	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0	1500.0	1500.0	1500.0
Temp, °C*	90	90	88	90	93	92
Viscosity, mPas*	26,500	28,650	24,800	28,250	42,650	31,250
Gel, °C	42	41	50-51	53	39	55
Melt, °C	60-65	62-67	60-61	70-74	60-63	65-69
PH	7.6	7.2	6.3	5.6	7.4	5.9
Cast Film						
Solids, est	40%	40%	40%	40%	38%	41%
BF (g)	<40	<40	<40	188	<40	185

	Ex 3-1	Ex 3-2	Ex 3-3	Ex 3-4	Ex 3-5	Ex 3-6
Ingredient (g)						
Dried film (2 hrs@ 40°C)						
Solids, est	66%	62%	63%	64%	62%	66%
BF (g)	370	248	445	1811	502	1265
Dried film (16 hours, 40 C)						
Solids, est	81%	79%	85%	80%	77%	80%
Avg film thickness (mm)	0.83	0.76	0.56	0.60	0.56	0.59
BF (g)	3826	4253	4144	7960	6918	8301

* Temperature and viscosity of the molten mass prior to casting

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some showed greater strengths than others.

Table VI reports compositions and properties of gel films prepared using blends of low viscosity guar ULV50 with sodium alginates. Protanal® LFR 5/60, Protanal® LF 20/40 and Protanal® SF 120 RB are sodium alginates available from FMC Corporation (Philadelphia, PA).

Table VI: Films Using Guar and Alginates

	Ex3-7	Ex 3-8	Ex 3-9
Ingredient (g)			
Water	836.3	836.3	836.3
LFR 5/60	40.5	0	0
LF 20/40	0	40.5	0
SF120 RB	0	0	30
Guar ULV50	49.5	49.5	45
Starch B760	220.8	220.8	220.8
M100	0	0	15.0
Sorbitol SP	264.4	264.4	264.4
Glycerin	88.2	88.2	88.2
Total weight	1500.0	1500.0	1500.0
Temp, °C*	90	94	93

	Ex3-7	Ex 3-8	Ex 3-9
Ingredient (g)			
Viscosity, mPas*	31,650	>50,000	>50,000
Gel, °C	50	NA	NA
Melt, °C	70-71	>95	>93
PH	5.6	5.5	5.6
Cast Film			
Solids, Brix	40%	40%	40%
BF (g)	<40	102	110
Dried film (2 hrs@ 40°C)			
Solids, est	60%	64%	67%
BF (g)	617	1250	1126
Dried film (16 hours, 40 C)			
Solids, est	80%	80%	94%
Avg film thickness (mm)	0.53	0.89	0.51
BF (g)	4780	7701	10,850

* Temperature and viscosity of the molten mass prior to casting

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some showed greater strengths than others.

Table VII presents compositions and gel films formed from low viscosity guar ULV 50 in combination with propylene glycol alginate. Protanal® ester BV4830 and Protanal® ester SLF3 are propylene glycol alginates available from FMC Corporation (Philadelphia PA) and Kibun, respectively.

Table VII: Films Using Low Viscosity Guar and Propylene Glycol Alginate

	Ex 3-10	Ex 3-11	Ex 3-12	Ex 3-13	Ex 3-14
Ingredient (g)					
Water	836.5	840.3	840.3	840.3	836.5
BV4830	12.0	0	91.2	0	12.0
SLF-3	0	85.5	0	114	0
HEC	0	1.8	1.9	2.4	0
Cgn L	40.5	0	24	0	40.5
Guar ULV50	37.5	30	0	NONE	37.5
B760	220.8	207.8	207.8	207.8	220.8

	Ex 3-10	Ex 3-11	Ex 3-12	Ex 3-13	Ex 3-14
Ingredient (g)					
M-100	0	0	0	0	
Na citrate	0	2.7	0	3.6	
K citrate	0	0	2.9	0	
KCl	0	0	2.4	0	
Sorbitol SP	264.4	248.8	248.8	248.8	264.4
Glycerin	88.2	83.0	83.0	83	88.2
Temp, °C	90	87	90	91	90
Viscosity, mPas	23,100	16,500	25,000	3250	23,100
Gel, °C	46	34-38	43-46	34-35	46
Melt, °C	60-68	62-64	56-62	58-60	60-68
pH	4.6	4.5	4.3	4.4	4.6
Cast Film					
Solids, Brix	41.5%	41	45%	39%	41.5%
BF (g)	147	,40	231	<40	147
Dried film (2 hrs@ 40°C)					
Solids, est	60%	65%	55%	74%	60%
BF (g)	592	355	842	1877	592
Dried film (16 hours, 40C)					
Solids, est	80%	77%	78%	85%	80%
Avg film thickness (mm)	0.62	0.60	0.75	0.67	0.62
BF (g)	7214	3317	9599	4677	7214

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some showed greater strengths than others.

Example 4: Fluid Mixing Apparatus of Figure 3

The following examples show films made using the fluid mixing apparatus of Figure 3. In these examples, Part A and Part B were pumped from separate holding tanks at ambient temperature, as two separate streams 4, 6, into two different inlet ports 42, 44 which fed the steam injection fluid mixing apparatus device 10. The two individual

streams 4, 6 were combined at the interface of the steam in the mixing zone 52 of the fluid mixing apparatus 10. The separate solutions of Part A and Part B were readily pumped into the fluid mixing apparatus 10 and mixed with steam 2. The steam 2 was introduced to the mixing zone at a pressure of 120 psi. The resulting molten mass or slurry mixture 8 flowed out of the exit port 56 of the fluid mixing apparatus 10. The mixture 8 was poured onto a smooth surface and drawn down to form a homogeneous film 9.

To measure the viscosity of the mixture 8, approximately 500 ml sample of the mixture 8 was collected from the outlet 56 and poured into a jar. The temperature, pH and viscosity were measured for this sample at 95°C. A Brookfield LVF viscometer was used to measure the viscosity. An appropriate speed and spindle combination were used such that a reading could be taken. The dial reading was converted to dynamic viscosity (cP).

To measure the film strength and solids level, the molten mass 8 was collected from the outlet 56 then cast using a draw down bar, with a gap set at 3 mm, onto a stainless steel metal plate. The initial films 9 or "fresh films" were collected. Portions of the fresh films 9 were dried by placing them in a 40°C forced air oven. Break force was measured on the cast and dried film strips using a Texture Analyzer TA-108S Mini Film Test Rig. The percent solids were determined by measuring the difference between the initial weight of the fresh film and the final weight of the dried films.

To measure the gel temperature, a portion of the molten mass 8 was collected from the outlet 56 of the mixing apparatus 10 and transferred to a test tube. Half of the test tube remained empty. A glass thermometer was inserted into the molten mass 8. The

material 8 was allowed to cool under room temperature conditions. After each degree of cooling, the thermometer was removed from the material 8. When a small, temporary indentation was observed in the surface of the mass 8, this temperature was recorded. The thermometer was re-inserted into the mass 8, which was allowed to cool further. The thermometer was removed and re-inserted at every degree of cooling until such a time as a permanent indentation formed in the mass 8, such that the indentation did not refill. The temperature at which the permanent indentation formed was recorded. The gel temperature reported was the range between the two recorded temperatures.

Table VIII - Mixtures Containing LV Guar

Example No.	4-1	4-2	4-3
Part A (%)			
Carrageenan 2	0	4.0	4.2
Carrageenan 1	4.3	0.0	0.0
ULV guar	4.6	4.9	5.1
Glycerin	33.5	33.5	27.0
Sorbitol	0.0	0.0	8.1
Part B (%)			
Starch	20.7	20.7	21.8
Water	36.9		
Mixing chamber temp. (°C)	108	108	108
Outlet temp (°C)	102	102	102
Viscosity cP (@95°C)	7900	7800	69000
PH	6.5	5.6	5.5
% solids	65	70	55
Gel temp. (°C)	60-65	46	>100
wet film strength (grams)	460	3402	921
dry film strength (grams)	5299	6587	9234

All the above formulations showed sufficient dry film strength for use in soft capsule manufacture, though some showed greater strengths than others.

The following Tables IX and X provides further descriptions of the components specified in the above examples.

Table IX - Component Descriptions

Name	Trade Name	Supplier	Description
low viscosity guar (LV guar)	Edicol ULV 50	Indian Gum Industries, Ltd.	
Glycerin		Callahan Chemical	99.70%
Sorbitol	Sorbo	SPI Polyols	70% sorbitol solution, USP/FCC
Starch	Pure-Cote B790	Grain Processing Corporation	

The following Table X provides a description of the various carrageenans used in this example.

Table X - Carrageenan Descriptions

Reference	Carrageenan Type	Description	Supplier
Carrageenan 1	Kappa	An alkali processed, clarified kappa-carrageenan extract of <i>Kappaphycus alvarezii</i> (<i>Eucheuma cottonii</i>) with low divalency	FMC Corporation
Carrageenan 2	low divalent kappa-2	An alkali processed, clarified, low divalency extract of <i>Gigartina skottsbergii</i> , essentially haploid (gametophyte) plants, such extract being commonly known as "kappa-2 carrageenan". Also includes minor levels (under 5% total) of lambda- and theta-carrageenans from diploid (tetrasporophyte) plants. Defined as the natural random block copolymer of kappa- and iota-carrageenans in the ratio of about 1.0 to 3.0:1 respectively,	FMC Corporation

		and has significantly different functionalities compared to mixing individual kappa- and iota-carrageenan natural polymers at the same ratio.	
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Example 11

Gel films were prepared using the following polymannan gums: konjac, locust bean gum (LBG) and CLBG/guar, a clarified blend of locust bean gum and guar (60/40 by weight). The kappa carrageenan viscosity is between 10 and 15 cps and the iota carrageenan had a Brookfield viscosity of 30-50 cps, respectively, when tested at 1.5% aqueous solution at 75°C. A dry premix was made of the gums. Distilled water and glycerin were weighed into a 1.2 liter stainless steel beaker. The dry premix was added to the water with good agitation, then heated to 90 °C and held within the temperature range 90°C to 95°C for 15 minutes to fully hydrate the gums. The hot solution was quickly poured into containers. Solution cast in petri dishes was cooled to room temperature to form films, then dried overnight in a forced draft oven at 45 °C to a constant weight. Film properties are reported in Table below.

TABLE XI: Polymannan Blend Formulations and Properties

	S	1	2	3	4
Ingredients (gm)					
Distilled water	195.0	195.0	195.0	195.0	195.0
Glycerin	50.0	50.0	50.0	50	50.0
Kappa cgn	1.90	1.65	3.50	1.65	1.65

Iota cgn	3.10	2.65	0	2.65	2.65
konjac	0	0.70	1.50	0	0
LBG	0	0	0	0.70	0
CLBG/guar	0	0	0	0	0.70
BF, gm	955	1218	3244	1796	1903
Penetration, cm	2.1	1.6	1.4	1.6	1.9
Rigidity	455	761	2317	1123	1002
Melt temp °C	36	43	39-43	49-52	45
Gel temp, °C	22	30	26	30	32

As described and demonstrated above, the films made in accordance with this invention can be used in conventional capsule making equipment previously used for making gelatin capsules. The hydrocolloid films produced by the present invention produce less waste and provide for easier processing than gelatin-based films.

While the invention has been described in detail and with reference to specific embodiments thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof.